Section of Anæsthetics

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High Pressure Oxygen

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Some Clinical and Experimental Applications of High Pressure Oxygen

Since about 1955 there has been a steadily increasing interest in the use of oxygen at pressures greater than atmospheric for a wide variety of human disorders. In London (Churchill-Davidson *et al.* 1955) single-patient chambers were designed for use in association with radiotherapy of cancer, while in Amsterdam and Glasgow, pressure vessels were constructed of a size large enough to house both patient and attendant medical and nursing staff (Boerema 1961, Illingworth *et al.* 1961). Only the patient breathes oxygen.

The working pressure of the existing Glasgow chamber is twice atmospheric; when 100% oxygen is used in anæsthetized patients this has the effect of raising the arterial oxygen tension in practice to 1,350–1,400 mmHg. In unanæsthetized volunteers, breathing oxygen through a standard BLB delivery mask with a flow rate of 8 litres per minute, the arterial Po_2 has been found to be about 750 mmHg. While greater arterial oxygen tensions could be achieved with higher ambient pressures, two atmospheres absolute was chosen in order to minimize the dangerous effects of prolonged administration of oxygen. In fact, this amount of oxygen has now been administered without untoward effect, in several conscious patients for periods of up to three days. During these prolonged exposures the oxygen mask is removed from the patient for half an hour every four to six hours, and at least once in twenty-four hours the chamber is decompressed to normal atmospheric pressure. These safety precautions are quite empirical but neither cerebral nor pulmonary complications have been detected.

Naturally with a new project of this variety many stones remain unturned and our experience in the treatment of anoxic anoxia is limited to some cases of pulmonary distress syndrome of the newborn. A few adult patients with respiratory collapse of various sorts have been treated in the pressure chamber but attention has been mainly focused on stagnant and anæmic anoxia. Carbon monoxide poisoning is the most obvious example of the latter and, while in Glasgow we have gained considerable experience of the treatment of this form of intoxication, Dr M E Sluijter of Amsterdam will deal with this aspect of the work in detail.

With reference to stagnant anoxia we have had an opportunity of dealing with both acute and chronic vascular disorders involving diminished blood flow to a part of the body. In acute obstruction of the arterial input the rationale of treatment in the pressure chamber is to increase the oxygen tension gradient between the sluggish blood flow and the anoxic cells and thus to raise the local tissue oxygen tension until an adequate collateral circulation has developed. Patients with this form of arterial occlusion therefore remain in the chamber breathing oxygen until there is clinical evidence of good collateral circulation or until it is clear that no further improvement is likely. This has required on occasions periods of more than seventy-two hours.

Table 1 shows the numbers and types of patients with traumatic ischæmia who have received hyperbaric oxygen therapy. In this type of condition no scientific assessment of the value of the treatment is possible because of the difficulty of carrying out a properly controlled clinical trial, but out of this varied group two patients have been chosen in whom it is reasonably certain that under normal methods of treatment greater loss of tissue might have been expected.

Table 1
Traumatic ischæmia–14 cases

	No. of cases
Multiple fractures of both lower limbs and pelvis	1
Osteofascial compartment compressions, leg and forearm	5
Traumatic amputation of foot	1
Cold injury, feet and hands	2
Cl. welchii infections of foot and leg	3
Degloving injury to both legs and left forearm	1
Almost complete avulsion of foot with replacement	1

Case 1 (Smith, Stevens, Griffiths & Ledingham 1961)
A boy with a compound fracture dislocation of the ankle. The anterior and posterior tibial vessels and the peroneal vessels were divided and there was extensive division of skin and soft tissue at the ankle level. Only two narrow strips of skin and the tendons remained to bridge the gap. It was possible to anastomose the two ends of the posterior tibial artery and this provided a tenuous blood supply.

Pressurization was commenced at this point and after twenty-four hours the oxygenation of the foot was much improved. The patient was maintained on hyperbaric oxygen for a total of ninety hours. The toes subsequently became gangrenous but a below-knee amputation had been avoided.

Case 2
An elderly woman with severe frostbite of both feet who had lost a toe the previous year under similar circumstances. On admission the fore part of each foot was obviously ischæmic and hyperbaric oxygen was administered for a total of seventy-two hours. The patient subsequently did very well and there was no loss of tissue.

In chronic obliterative vascular disorders the problem is more difficult. There is certainly no indication that the pressure chamber will alter the long-term outlook for these patients. Some of them, however, eventually come to amputation because of intractable ulcers and painful ischæmic neuritis and it is in this group that a degree of success has been achieved. Hyperbaric oxygen is administered for a few hours per day for two to three weeks and in some cases relief of pain has occurred quite dramatically. An analysis of the outcome in 23 such patients is shown in Table 2.

Satisfactory results were obtained in 7 younger patients who had chronic ischæmic ulcers typical of thromboangiitis obliterans. One of these had an ulcer which proved unresponsive to all forms of therapy for six months, part of which was spent in hospital. Following three weeks of intermittent hyperoxygenation the ulcer was almost completely healed and did not subsequently break down.

Another form of atherosclerotic vascular disease which should theoretically respond to treatment in the pressure chamber is myocardial infarction. Professor Smith's experimental work in dogs (Smith & Lawson 1962) by ligation of the left circumflex coronary vessel has lent support to this hypothesis. In view of the demands on the chamber for other activities we have had to delay clinical observation on myocardial infarction until recently, but during the past few months a long-term clinical trial has begun.

Table 2
Chronic arterial insufficiency – 23 cases

	No. of cases		
Major ischæmic neuropathy and tissue necrosis:	8		
Major amputation		4	
Pain subsided		4	2 with loss of toes 2 with intact skin
Minor ischæmic neuropathy with or without tissue necrosis:	15		
Minor amputation		5	
Healing or no loss of tissue		10	

The plan is to assess all patients presenting with coronary vascular disease and to admit alternate cases with definite electrocardiographic evidence of an infarct to the pressure chamber for three days. A control group of patients will receive as near as possible similar supervision in the ward. It would be valueless to discuss the results of the trial at this early stage as the numbers are too small for analysis.

In the specialized form of anoxic anoxia seen in the pulmonary distress syndrome of the newborn or 'hyaline membrane disease' the transport of oxygen across the alveolar membrane is obstructed by a noncellular eosinophilic coagulum filling the pulmonary alveoli. The fatal outcome in a large proportion of these infants is due partly to anoxia and partly to an associated metabolic acidosis. Although treatment by placing these infants in an incubator within the pressure chamber relieved the anoxia, there was at first little improvement in mortality and it was only when careful serial correction of the acid-base disturbance was carried out in addition, that dramatic improvement in the results occurred – in fact reversing a 66% mortality to a 66% survival rate (Hutchison *et al.* 1962).

Experimental Work
The first study which provoked interest was the possibility of increasing the period of total arrest of the circulation without producing neurological damage by supersaturating the tissues with oxygen prior to the period of arrest. Clinically this would give the surgeon an added safety factor during any intracardiac procedure involving total circulatory arrest, especially in cyanotic heart disease.

Oxygen at normal pressure and at two atmospheres has been compared in two large groups of dogs. Circulatory standstill is accomplished by thoracotomy and occlusion of the inflow and outflow tracts of the heart. At the end of the predetermined period of arrest, the circulation is re-established and the animal recovered to assess its neurological state. By this means it has been possible to estimate the period of safe arrest of the circulation in the two groups, the term 'safe' indicating consistent prompt and efficient recovery of the myocardium without subsequent neurological damage in the survivors. These experiments have been performed at normal body temperatures, at moderate hypothermia (27°C ± 1°C) and at deeper hypothermia (20°C ± 1°C); the

Table 3
Comparison of maximum periods of safe arrest of the circulation

	Duration of arrest (min)	
Temperature	*1 ATA*	*2 ATA*
37°C	5	8
28°C	20	30
20°C	30–35	40–45

ATA = atmospheres absolute

results are seen in Table 3. The beneficial effects of hyperbaric oxygen breathing can be seen at each of these temperatures.

The technique used in the deep hypothermic series can best be illustrated by reference to the experimental protocol of one of the animals in the 20°C group (Fig 1). Anæsthesia is induced with sodium thiopentone and light anæsthesia is maintained with halothane and oxygen. A positive pressure ventilator is adjusted until the arterial P_{CO_2} has been fixed at approximately 40 mmHg using the micro-Astrup apparatus. Thereafter ventilation is not altered. The animal is cooled with a mixture of ice and water (at 5°C) to 20°C, suxamethonium being used to prevent shivering. Halothane anæsthesia is stopped at 30°C during the cooling phase. When the required temperature has been reached thoracotomy is carried out and the circulation arrested. After re-establishment of the circulation at the end of the arrest the chest is formally closed and the animal rewarmed. The points of note in this technique are the relatively quick cooling (averaging three-quarters of an hour), the avoidance of any degree of hypotension, the avoidance of metabolic acidosis throughout the procedure except that occurring as a result of the period of arrest, and the rapid onset of an adequate blood pressure following circulatory standstill. Ventricular fibrillation has never occurred during the cooling phase of these experiments and if it occurs at the end of the arrest electrical defibrillation is achieved with ease. No ventricular fibrillation has occurred during the rewarming phase. With the experiments at normal body temperature it was found that total circulatory arrest produced a metabolic acidosis of 1 mEq per litre of blood per minute of arrest. Using this information sodium bicarbonate was administered immediately before the arrest in a dose calculated to neutralize the anoxic metabolic acid production of the arrest; this resulted in a much quicker establishment of adequate cardiac output and as a result the twenty-four hour post-operative condition of the animals was much improved (Ledingham & Norman 1962). The effect of the administration of the sodium bicarbonate on the metabolic acid base measurement is seen in Fig 2 as compared with a control animal which did not receive alkali.

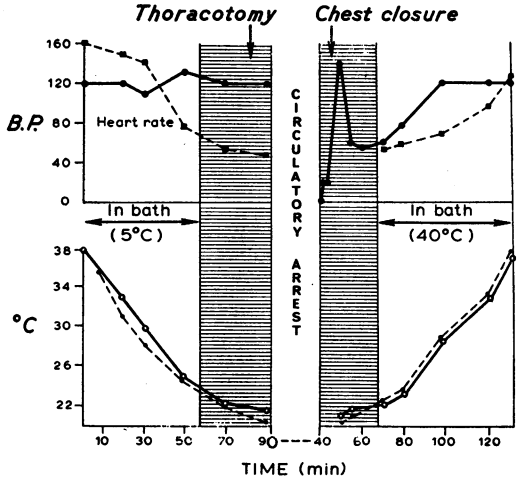

Fig 1 *Experimental procedure in dog (L15); 40 min arrest.* ●—● *B.P. mm Hg;* ■---■ *heart rate beats/min;* ○—○ *mid-œsophageal temperature;* ●---● *rectal temperature (deg. C)*

Investigation of the role of various alkalis in a similar manner is in progress in the hypothermic series.

The results of this study are encouraging and with certain modifications it is felt that the technique could be readily adapted to open-heart surgery of the infant and young child where surface cooling is efficient. With the collaboration of a team of cardiothoracic surgeons in Glasgow this possibility is being explored.

Another experimental investigation in progress at present is the study of cerebral blood flow in relation to exposure to high atmospheric oxygen. Naturally it will be important to evaluate the role of oxygen at high pressure in the treatment of human cerebrovascular injury and disease but, because of the apparent susceptibility of the

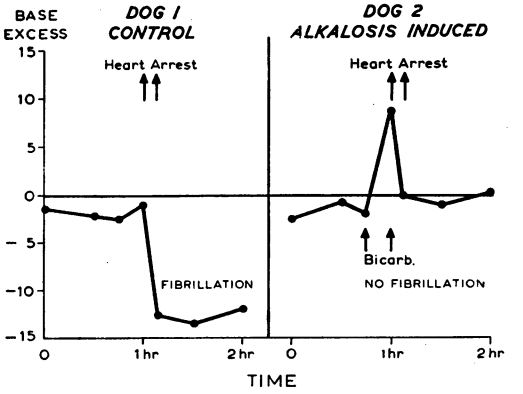

Fig 2 *Prevention of arrhythmia after cardiac arrest. Effect of pre-arrest administration of sodium bicarbonate. Base excess units mEq/l*

cerebral vessels to vasoconstriction under these conditions (Lambertsen *et al.* 1953), it was felt important to obtain more experimental data before subjecting patients to this form of therapy.

Some preliminary experiments (Smith, Lawson, Renfrew, Ledingham & Sharp 1961) showed that when the carotid and vertebral arteries at the root of the neck were occluded in the dog the EEG flattened within three-quarters of a minute when the animal was breathing air at normal pressure. When this procedure was repeated with the animal breathing oxygen at two atmospheres the EEG remained, for all practical purposes, unchanged. One of the conclusions drawn from this experiment was that if cerebral vasoconstriction did take place with oxygen at high pressure it was not enough to negate the beneficial effects of thus increasing the arterial Po_2.

The next problem was to obtain quantitative data for cerebral blood flow in animals breathing air and oxygen at one and two atmospheres. Sokoloff (1959) has pointed out that a high arterial Po_2 at normal pressure causes cerebral vasoconstriction leading to a reduction in cerebral blood flow of about 12% to 15%. In experiments performed in this department, Jacobson, Harper, Lawson, McDowall & Norman (personal communication, 1963) using the krypton 85 clearance technique of Lassen & Ingvar (1961, Ingvar & Lassen 1962) could not demonstrate any further quantitive vasoconstriction with oxygen at two atmospheres. Intravenous sodium thiopentone was used as the anæsthetic agent in these animals and it may be that this agent, known to produce cerebral vasoconstriction by itself (Pierce *et al.* 1962), may have obscured the effect of oxygen at high pressure. Other anæsthetic agents are therefore being investigated to obtain more complete information.

One of the subjects which necessarily attracts close attention is that of prolonged administration of hyperbaric oxygen. This has been described as falling into two categories – neurological and pulmonary. Although oxygen at two atmospheres is not associated with convulsions in animals there are many reports of pulmonary damage occurring at this pressure in most animals. In this department McDowall & Karasewich (personal communication, 1963) have shown that conscious dogs exposed to 90% oxygen at two atmospheres die between ten and fourteen hours and that at autopsy their lungs are intensely congested and contain small areas of collapse with much frothy blood-stained mucus in the distal bronchioles. McDowall has further demonstrated that by anæsthetizing dogs with halothane and oxygen at high pressure using intermittent positive pressure respiration no lung changes are observed over the same period of time. The conclusion therefore drawn is that either halothane or intermittent positive pressure respiration prevents the damaging effect of oxygen at high pressure on the dog lung for this period of exposure. While this study as it stands at the moment does not greatly further our knowledge, extension of the work in this field is vital if the basic ætiology of oxygen poisoning is to be elucidated. It must be remembered that against this background of animal oxygen intoxication no patient so far exposed has shown either cerebral or pulmonary side-effects directly attributable to the oxygen administration.

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The Treatment of Carbon Monoxide Poisoning by Administration of Oxygen at High Atmospheric Pressure

During the period December 1960 to August 1962 all patients with a diagnosis of carbon monoxide intoxication who were brought into the Wilhelmina Gasthuis in Amsterdam were treated in the pressure chamber with administration of oxygen at a pressure of 3 atmospheres absolute (ATA). In all 40 patients were treated in this period. The cause of the intoxication in these patients is shown in Table 1.

On admission we divided our patients into three clinical groups. Group 1 contains 21 patients who were conscious or lightly comatose on admission; these patients had no hypotension, respiratory depression or neurological abnormality. Table 2 shows the frequency of the signs and symptoms that were present. Group 2 contains

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